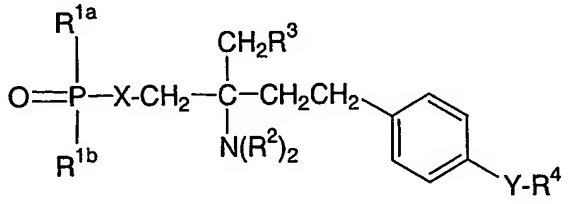
WHAT IS CLAIMED IS:

1. A method of treating an immunoregulatory abnormality in a mammalian patient in need of such treatment comprising administering to said patient a compound which is an agonist of the $S1P_1$/Edg1 receptor in an amount effective for treating said immunoregulatory abnormality, wherein said compound possesses a selectivity for the S1P1/Edg1 receptor over the S1PR3/Edg3 receptor of at least 20 fold as measured by the ratio of EC_{50} for the $S1P_1$/Edg1 receptor to the EC_{50} for the $S1P_3$/Edg3 receptor as evaluated in the ^{35}S-GTPγS binding assay and wherein said compound possesses an EC_{50} for binding to the $S1P_1$/Edg1 receptor of 100 nM or less as evaluated by the ^{35}S-GTPγS binding assay,

with the proviso that the compound does not fall within formula A:



A

or a pharmaceutically acceptable salt or hydrate thereof, wherein:

X is O, S, NR^1 or $(CH_2)_{1-2}$, optionally substituted with 1-4 halo groups;

R^1 is H, C_{1-4}alkyl or haloC_{1-4} alkyl;

R^{1a} is H, OH, C_{1-4}alkyl, or OC_{1-4} alkyl, the alkyl and alkyl portions being optionally substituted with 1-3 halo groups;

R^{1b} represents H, OH, C_{1-4} alkyl or haloC_{1-4} alkyl;

each R^2 is independently selected from the group consisting of: H, C_{1-4} alkyl and haloC_{1-4} alkyl,

R^3 is H, OH, halo, C_{1-4}alkyl, OC_{1-4}alkyl, O-haloC_{1-4}alkyl or hydroxyC_{1-4}alkyl,

Y is selected from the group consisting of: $-CH_2-$, -C(O)-, -CH(OH)-, -C(=NOH)-, O and S, and

R^4 is selected from the group consisting of: C_{4-14}alkyl and C_{4-14}alkenyl.

2. The method according to Claim 1 wherein the compound has a selectivity for the $S1P_1$/Edg1 receptor over the $S1P_3$/Edg3 receptor of at least 100 fold as measured by the ratio of EC_{50} for the $S1P_1$/Edg1 receptor to the EC_{50} for the $S1P_3$/Edg3 receptor as evaluated in the ^{35}S-GTPγS binding assay.

3. The method according to Claim 2 wherein the compound has a selectivity for the $S1P_1$/Edg1 receptor over the $S1P_3$/Edg3 receptor of at least 200 fold as measured by the ratio of EC_{50} for the $S1P_1$/Edg1 receptor to the EC_{50} for the $S1P_3$/Edg3 receptor as evaluated in the ^{35}S-GTPγS binding assay.

4. The method according to Claim 3 wherein the compound has a selectivity for the $S1P_1$/Edg1 receptor over the $S1P_3$/Edg3 receptor of at least 500 fold as measured by the ratio of EC_{50} for the $S1P_1$/Edg1 receptor to the EC_{50} for the $S1P_3$/Edg3 receptor as evaluated in the ^{35}S-GTPγS binding assay.

5. The method according to Claim 4 wherein the compound has a selectivity for the $S1P_1$/Edg1 receptor over the $S1P_3$/Edg3 receptor of at least 2000

fold as measured by the ratio of EC_{50} for the $S1P_1$/Edg1 receptor to the EC_{50} for the $S1P_3$/Edg3 receptor as evaluated in the ^{35}S-GTPγS binding assay.

6. A method of treating an immunoregulatory abnormality in a mammalian patient in need of such treatment comprising administering to said patient a compound which is an agonist of the $S1P_1$/Edg1 receptor in an amount effective for treating said immunoregulatory abnormality, wherein said compound possesses a selectivity for the S1P1/Edg1 receptor over the $S1P_3$/Edg3 receptor of at least 100 fold as measured by the ratio of EC_{50} for the $S1P_1$/Edg1 receptor to the EC_{50} for the $S1P_3$/Edg3 receptor as evaluated in the ^{35}S-GTPγS binding assay and wherein said compound possesses an EC_{50} for binding to the $S1P_1$/Edg1 receptor of 10 nM or less as evaluated by the ^{35}S-GTPγS binding assay.

7. The method according to Claim 6 wherein the compound possesses an EC_{50} for binding to the $S1P_1$/Edg1 receptor of 1 nM or less as evaluated by the ^{35}S-GTPγS binding assay.

8. The method according to Claim 6 wherein the compound has a selectivity for the $S1P_1$/Edg1 receptor over the $S1P_3$/Edg3 receptor of at least 200 fold as measured by the ratio of EC_{50} for the $S1P_1$/Edg1 receptor to the EC_{50} for the $S1P_3$/Edg3 receptor as evaluated in the ^{35}S-GTPγS binding assay.

9. The method according to Claim 8 wherein the compound has a selectivity for the $S1P_1$/Edg1 receptor over the $S1P_3$/Edg3 receptor of at least 500 fold as measured by the ratio of EC_{50} for the $S1P_1$/Edg1 receptor to the EC_{50} for the $S1P_3$/Edg3 receptor as evaluated in the ^{35}S-GTPγS binding assay.

10. The method according to Claim 9 wherein the compound has a selectivity for the $S1P_1$/Edg1 receptor over the $S1P_3$/Edg3 receptor of at least 1000 fold as measured by the ratio of EC_{50} for the $S1P_1$/Edg1 receptor to the EC_{50} for the $S1PR_3$/Edg3 receptor as evaluated in the ^{35}S-GTPγS binding assay.

11. The method according to Claim 10 wherein the compound has a selectivity for the S1P1/Edg1 receptor over the S1PR3/Edg3 receptor of at least 2000 fold as measured by the ratio of EC_{50} for the S1P1/Edg1 receptor to the EC_{50} for the S1P3/Edg3 receptor as evaluated in the ^{35}S-GTPγS binding assay.

12. The method according to Claim 1 wherein the immunoregulatory abnormality is an autoimmune or chronic inflammatory disease selected from the group consisting of: systemic lupus erythematosis, chronic rheumatoid arthritis, type I diabetes mellitus, inflammatory bowel disease, biliary cirrhosis, uveitis, multiple sclerosis, Crohn's disease, ulcerative colitis, bullous pemphigoid, sarcoidosis, psoriasis, autoimmune myositis, Wegener's granulomatosis, ichthyosis, Graves ophthalmopathy and asthma.

13. The method according to Claim 1 wherein the immunoregulatory abnormality is bone marrow or organ transplant rejection or graft-versus-host disease.

14. The method according to Claim 1 wherein the immunoregulatory abnormality is selected from the group consisting of: transplantation of organs or tissue, graft-versus-host diseases brought about by transplantation, autoimmune syndromes including rheumatoid arthritis, systemic lupus erythematosus, Hashimoto's thyroiditis, multiple sclerosis, myasthenia gravis, type I diabetes, uveitis, posterior uveitis, allergic encephalomyelitis, glomerulonephritis, post-infectious autoimmune diseases including rheumatic fever and post-infectious glomerulonephritis, inflammatory and hyperproliferative skin diseases, psoriasis, atopic dermatitis, contact dermatitis, eczematous dermatitis, seborrhoeic dermatitis, lichen planus, pemphigus, bullous pemphigoid, epidermolysis bullosa, urticaria, angioedemas, vasculitis, erythema, cutaneous eosinophilia, lupus erythematosus, acne, alopecia areata, keratoconjunctivitis, vernal conjunctivitis, uveitis associated with Behcet's disease, keratitis, herpetic keratitis, conical cornea, dystrophia epithelialis corneae, corneal leukoma, ocular pemphigus, Mooren's ulcer, scleritis, Graves' opthalmopathy, Vogt-Koyanagi-Harada syndrome, sarcoidosis, pollen allergies,

reversible obstructive airway disease, bronchial asthma, allergic asthma, intrinsic asthma, extrinsic asthma, dust asthma, chronic or inveterate asthma, late asthma and airway hyper-responsiveness, bronchitis, gastric ulcers, vascular damage caused by ischemic diseases and thrombosis, ischemic bowel diseases, inflammatory bowel diseases, necrotizing enterocolitis, intestinal lesions associated with thermal burns, coeliac diseases, proctitis, eosinophilic gastroenteritis, mastocytosis, Crohn's disease, ulcerative colitis, migraine, rhinitis, eczema, interstitial nephritis, Goodpasture's syndrome, hemolytic-uremic syndrome, diabetic nephropathy, multiple myositis, Guillain-Barre syndrome, Meniere's disease, polyneuritis, multiple neuritis, mononeuritis, radiculopathy, hyperthyroidism, Basedow's disease, pure red cell aplasia, aplastic anemia, hypoplastic anemia, idiopathic thrombocytopenic purpura, autoimmune hemolytic anemia, agranulocytosis, pernicious anemia, megaloblastic anemia, anerythroplasia, osteoporosis, sarcoidosis, fibroid lung, idiopathic interstitial pneumonia, dermatomyositis, leukoderma vulgaris, ichthyosis vulgaris, photoallergic sensitivity, cutaneous T cell lymphoma, chronic lymphocytic leukemia, arteriosclerosis, atherosclerosis, aortitis syndrome, polyarteritis nodosa, myocardosis, scleroderma, Wegener's granuloma, Sjogren's syndrome, adiposis, eosinophilic fascitis, lesions of gingiva, periodontium, alveolar bone, substantia ossea dentis, glomerulonephritis, male pattern alopecia or alopecia senilis by preventing epilation or providing hair germination and/or promoting hair generation and hair growth, muscular dystrophy, pyoderma and Sezary's syndrome, Addison's disease, ischemia-reperfusion injury of organs which occurs upon preservation, transplantation or ischemic disease, endotoxin-shock, pseudomembranous colitis, colitis caused by drug or radiation, ischemic acute renal insufficiency, chronic renal insufficiency, toxinosis caused by lung-oxygen or drugs, lung cancer, pulmonary emphysema, cataracta, siderosis, retinitis pigmentosa, senile macular degeneration, vitreal scarring, corneal alkali burn, dermatitis erythema multiforme, linear IgA ballous dermatitis and cement dermatitis, gingivitis, periodontitis, sepsis, pancreatitis, diseases caused by environmental pollution, aging, carcinogenesis, metastasis of carcinoma and hypobaropathy, disease caused by histamine or leukotriene-C4 release, Behcet's disease, autoimmune hepatitis, primary biliary cirrhosis, sclerosing cholangitis, partial liver resection, acute liver necrosis, necrosis caused by toxin, viral hepatitis, shock, or anoxia, B-virus hepatitis, non-A/non-B hepatitis, cirrhosis, alcoholic cirrhosis, hepatic

failure, fulminant hepatic failure, late-onset hepatic failure, "acute-on-chronic" liver failure, augmentation of chemotherapeutic effect, cytomegalovirus infection, HCMV infection, AIDS, cancer, senile dementia, trauma, and chronic bacterial infection.

15. The method according to Claim 1 wherein the immunoregulatory abnormality is multiple sclerosis.

16. The method according to Claim 1 wherein the immunoregulatory abnormality is rheumatoid arthritis.

17. The method according to Claim 1 wherein the immunoregulatory abnormality is systemic lupus erythematosus.

18. The method according to Claim 1 wherein the immunoregulatory abnormality is psoriasis.

19. The method according to Claim 1 wherein the immunoregulatory abnormality is rejection of transplanted organ or tissue.

20. The method according to Claim 1 wherein the immunoregulatory abnormality is inflammatory bowel disease.

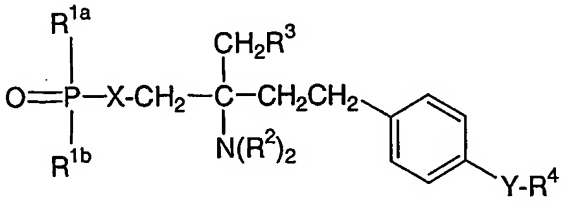
21. The method according to Claim 1 wherein the immunoregulatory abnormality is a malignancy of lymphoid origin.

22. The method according to Claim 21 wherein the immunoregulatory abnormality is acute and chronic lymphocytic leukemias and lymphomas.

23. A pharmaceutical composition comprised of a compound which is an agonist of the $S1P_1$/Edg1 receptor in an amount effective for treating an immunoregulatory abnormality, wherein said compound possesses a selectivity for the S1P1/Edg1 receptor over the $S1PR_3$/Edg3 receptor of at least 20 fold as measured by

the ratio of EC_{50} for the $S1P_1$/Edg1 receptor to the EC_{50} for the $S1P_3$/Edg3 receptor as evaluated in the ^{35}S-GTPγS binding assay and wherein said compound possesses an EC_{50} for binding to the $S1P_1$/Edg1 receptor of 100 nM or less as evaluated by the ^{35}S-GTPγS binding assay,

with the proviso that the compound does not fall within formula A:



A

or a pharmaceutically acceptable salt or hydrate thereof, wherein:

X is O, S, NR^1 or $(CH_2)_{1-2}$, optionally substituted with 1-4 halo groups;

R^1 is H, C_{1-4}alkyl or haloC_{1-4} alkyl;

R^{1a} is H, OH, C_{1-4}alkyl, or OC_{1-4} alkyl, the alkyl and alkyl portions being optionally substituted with 1-3 halo groups;

R^{1b} represents H, OH, C_{1-4} alkyl or haloC_{1-4} alkyl;

each R^2 is independently selected from the group consisting of: H, C_{1-4} alkyl and haloC_{1-4} alkyl,

R^3 is H, OH, halo, C_{1-4}alkyl, OC_{1-4}alkyl, O-haloC_{1-4}alkyl or hydroxyC_{1-4}alkyl,

Y is selected from the group consisting of: $-CH_2-$, -C(O)-, -CH(OH)-, -C(=NOH)-, O and S, and

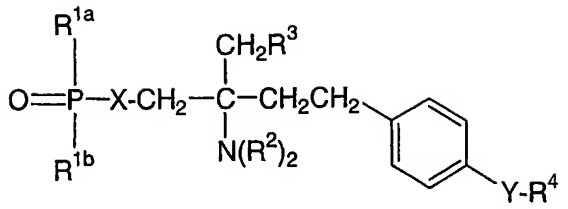
R^4 is selected from the group consisting of: C_{4-14}alkyl and C_{4-14}alkenyl,

in combination with a pharmaceutically acceptable carrier.

24. A pharmaceutical composition comprised of a compound which is an agonist of the $S1P_1$/Edg1 receptor in an amount effective for treating an immunoregulatory abnormality, wherein said compound possesses a selectivity for the S1P1/Edg1 receptor over the S1PR3/Edg3 receptor of at least 100 fold as measured by the ratio of EC_{50} for the $S1P_1$/Edg1 receptor to the EC_{50} for the $S1P_3$/Edg3 receptor as evaluated in the ^{35}S-GTPγS binding assay and wherein said compound possesses an EC_{50} for binding to the $S1P_1$/Edg1 receptor of 10 nM or less as evaluated by the ^{35}S-GTPγS binding assay, in combination with a pharmaceutically acceptable carrier.

25. A method of identifying a candidate compound which is an agonist of the $S1P_1$/Edg1 receptor that is selective over the $S1P_3$/Edg3 receptor, wherein said candidate compound possesses a selectivity for the $S1P_1$/Edg1 receptor over the $S1P_3$/Edg3 receptor of at least 20 fold as measured by the ratio of EC_{50} for the $S1P_1$/Edg1 receptor to the EC_{50} for the $S1P_3$/Edg3 receptor as evaluated in the ^{35}S-GTPγS binding assay and wherein said candidate compound possesses an EC_{50} for binding to the $S1P_1$/Edg1 receptor of 100 nM or less as evaluated by the ^{35}S-GTPγS binding assay,

with the proviso that the candidate compound does not fall within formula A:



A

or a pharmaceutically acceptable salt or hydrate thereof, wherein:

X is O, S, NR^1 or $(CH_2)_{1-2}$, optionally substituted with 1-4 halo groups;

R^1 is H, C_{1-4}alkyl or haloC_{1-4} alkyl;

R^{1a} is H, OH, C_{1-4}alkyl, or OC_{1-4} alkyl, the alkyl and alkyl portions being optionally substituted with 1-3 halo groups;

R^{1b} represents H, OH, C_{1-4} alkyl or haloC_{1-4} alkyl;

each R^2 is independently selected from the group consisting of: H, C_{1-4} alkyl and haloC_{1-4} alkyl,

R^3 is H, OH, halo, C_{1-4}alkyl, OC_{1-4}alkyl, O-haloC_{1-4}alkyl or hydroxyC_{1-4}alkyl,

Y is selected from the group consisting of: $-CH_2-$, -C(O)-, -CH(OH)-, -C(=NOH)-, O and S, and

R^4 is selected from the group consisting of: C_{4-14}alkyl and C_{4-14}alkenyl,

comprising:

(1) providing a first receptor preparation comprising:
(a) a recombinant cell expressing the $S1P_1$/Edg1 receptor or a functional equivalent of the $S1P_1$/Edg1 receptor capable of binding to sphingosine-1-phosphate ("S1P"); or
(b) a membrane preparation of a recombinant cell in accordance with subsection (1)(a);

(2) providing a second receptor preparation comprising:
(a) a recombinant cell expressing the $S1P_3$/Edg3 receptor or a functional equivalent of the $S1P_3$/Edg3 receptor capable of binding to sphingosine-1-phosphate ("S1P"); or
(b) a membrane preparation of a recombinant cell in accordance with subsection (2)(a);

(3) separately contacting said cells or membrane preparations with the candidate compound; and

(4) determining whether the candidate compound binds to and activates the $S1P_1$/Edg1 and $S1P_3$/Ed3 receptors by measuring the level of a signal generated from the interaction of the candidate compound with each receptor, thereby indicating whether the candidate compound is an agonist of the $S1P_1$/Edg1 receptor that is selective over the $S1P_3$/Edg3 receptor.

26. A method in accordance with claim 25 wherein the method further comprises conducting the method in the presence of labeled or unlabeled S1P, di-hydro S1P or a ligand for the S1P1/Edg1 and/or S1P3/Edg3 receptor; provided that if a ligand is utilized that is specific for either the S1P1/Edg1 or S1P3/Edg3 receptor, the receptor ligand utilized in the first receptor preparation is a ligand of the S1P1/Edg1 receptor and the ligand utilized in the second receptor preparation is a ligand of the S1P3/Edg3 receptor; and provided, further, that the method would additionally comprise measuring the level of a signal generated from the interaction of the S1P, di-

hydro S1P or ligand; wherein a compound that effects a reduction of the signal from the interaction of the S1P, di-hydro S1P or ligand, with the receptor and activates the S1P1/Edg1 receptor at a greater level than that obtained at the S1P3/Edg3 receptor is a selective agonist of the S1P1/Edg1 receptor.

27. A method in accordance with claim 25 wherein the signal indicates extracellular pH changes caused by receptor activation.

28. A method in accordance with claim 25 wherein the signal indicates levels of cAMP present within the cell.

29. A method in accordance with claim 25 wherein the signal indicates adenylate cyclase accumulation.

30. A method in accordance with claim 25 wherein the signal indicates Ca+ flux.

31. The method according to Claim 25 wherein the candidate compound has a selectivity for the $S1P_1$/Edg1 receptor over the $S1P_3$/Edg3 receptor of at least 100 fold as measured by the ratio of EC_{50} for the $S1P_1$/Edg1 receptor to the EC_{50} for the $S1P_3$/Edg3 receptor as evaluated in the ^{35}S-GTPγS binding assay.

32. The method according to Claim 31 wherein the candidate compound has a selectivity for the $S1P_1$/Edg1 receptor over the $S1P_3$/Edg3 receptor of at least 200 fold as measured by the ratio of EC_{50} for the $S1P_1$/Edg1 receptor to the EC_{50} for the $S1P_3$/Edg3 receptor as evaluated in the ^{35}S-GTPγS binding assay.

33. The method according to Claim 32 wherein the candidate compound has a selectivity for the $S1P_1$/Edg1 receptor over the $S1P_3$/Edg3 receptor of at least 500 fold as measured by the ratio of EC_{50} for the $S1P_1$/Edg1 receptor to the EC_{50} for the $S1P_3$/Edg3 receptor as evaluated in the ^{35}S-GTPγS binding assay.

34. The method according to Claim 33 wherein the candidate compound has a selectivity for the S1P1/Edg1 receptor over the S1P3/Edg3 receptor of at least 2000 fold as measured by the ratio of EC_{50} for the S1P1/Edg1 receptor to the EC_{50} for the S1P3/Edg3 receptor as evaluated in the ^{35}S-GTPγS binding assay.

35. The method according to Claim 25 wherein the candidate compound possesses an EC_{50} for binding to the S1P1/Edg1 receptor of 1 nM or less as evaluated by the ^{35}S-GTPγS binding assay.

36. A method of identifying a candidate compound which is an agonist of the S1P1/Edg1 receptor that is selective over the S1P3/Edg3 receptor, wherein said candidate compound possesses a selectivity for the S1P1/Edg1 receptor over the S1P3/Edg3 receptor of at least 100 fold as measured by the ratio of EC_{50} for the S1P1/Edg1 receptor to the EC_{50} for the S1P3/Edg3 receptor as evaluated in the ^{35}S-GTPγS binding assay and wherein said candidate compound possesses an EC_{50} for binding to the S1P1/Edg1 receptor of 10 nM or less as evaluated by the ^{35}S-GTPγS binding assay, comprising:

(1) providing a first receptor preparation comprising:
   (a) a recombinant cell expressing the S1P1/Edg1 receptor or a functional equivalent of the S1P1/Edg1 receptor capable of binding to sphingosine-1-phosphate ("S1P"); or
   (b) a membrane preparation of a recombinant cell in accordance with subsection (1)(a);

(2) providing a second receptor preparation comprising:
   (a) a recombinant cell expressing the S1P3/Edg3 receptor or a functional equivalent of the S1P3/Edg3 receptor capable of binding to sphingosine-1-phosphate ("S1P"); or
   (b) a membrane preparation of a recombinant cell in accordance with subsection (2)(a);

(3) separately contacting said cells or membrane preparations with the candidate compound; and

(4) determining whether the candidate compound binds to and activates the $S1P_1$/Edg1 and $S1P_3$/Ed3 receptors by measuring the level of a signal generated from the interaction of the candidate compound with each receptor, thereby indicating whether the candidate compound is an agonist of the $S1P_1$/Edg1 receptor that is selective over the $S1P_3$/Edg3 receptor.

37. A method in accordance with claim 36 wherein the method further comprises conducting the method in the presence of labeled or unlabeled S1P, di-hydro S1P or a ligand for the S1P1/Edg1 and/or S1P3/Edg3 receptor; provided that if a ligand is utilized that is specific for either the S1P1/Edg1 or S1P3/Edg3 receptor, the receptor ligand utilized in the first receptor preparation is a ligand of the S1P1/Edg1 receptor and the ligand utilized in the second receptor preparation is a ligand of the S1P3/Edg 3 receptor; and provided, further, that the method would additionally comprise measuring the level of a signal generated from the interaction of the S1P, di-hydro S1P or ligand; wherein a compound that effects a reduction of the signal from the interaction of the S1P, di-hydro S1P or ligand, with the receptor and activates the SIP1/Edg1 receptor at a greater level than that obtained at the S1P3/Edg3 receptor is a selective agonist of the SIP1/Edg1 receptor.

38. A method in accordance with claim 36 wherein the signal indicates extracellular pH changes caused by receptor activation.

39. A method in accordance with claim 36 wherein the signal indicates levels of cAMP present within the cell.

40. A method in accordance with claim 36 wherein the signal indicates adenylate cyclase accumulation.

41. A method in accordance with claim 36 wherein the signal indicates Ca+ flux.

42. The method according to Claim 36 wherein the candidate compound has a selectivity for the $S1P_1$/Edg1 receptor over the S1P3/Edg3 receptor of at least 200 fold as measured by the ratio of EC_{50} for the $S1P_1$/Edg1 receptor to the EC_{50} for the S1P3/Edg3 receptor as evaluated in the ^{35}S-GTPγS binding assay.

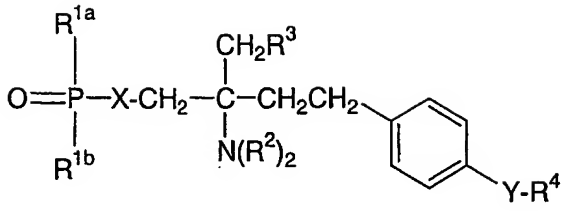
43. The method according to Claim 42 wherein the candidate compound has a selectivity for the $S1P_1$/Edg1 receptor over the S1P3/Edg3 receptor of at least 500 fold as measured by the ratio of EC_{50} for the $S1P_1$/Edg1 receptor to the EC_{50} for the S1P3/Edg3 receptor as evaluated in the ^{35}S-GTPγS binding assay.

44. The method according to Claim 43 wherein the candidate compound has a selectivity for the $S1P_1$/Edg1 receptor over the S1P3/Edg3 receptor of at least 1000 fold as measured by the ratio of EC_{50} for the $S1P_1$/Edg1 receptor to the EC_{50} for the S1PR3/Edg3 receptor as evaluated in the ^{35}S-GTPγS binding assay.

45. The method according to Claim 44 wherein the candidate compound has a selectivity for the $S1P_1$/Edg1 receptor over the S1P3/Edg3 receptor of at least 2000 fold as measured by the ratio of EC_{50} for the $S1P_1$/Edg1 receptor to the EC_{50} for the S1P3/Edg3 receptor as evaluated in the ^{35}S-GTPγS binding assay.

46. A method of treating a respiratory disease or condition in a mammalian patient in need of such treatment comprising administering to said patient a compound which is an agonist of the $S1P_1$/Edg1 receptor in an amount effective for treating said respiratory disease or condition, wherein said compound possesses a selectivity for the S1P1/Edg1 receptor over the S1PR3/Edg3 receptor of at least 20 fold as measured by the ratio of EC_{50} for the $S1P_1$/Edg1 receptor to the EC_{50} for the S1P3/Edg3 receptor as evaluated in the ^{35}S-GTPγS binding assay and wherein said compound possesses an EC_{50} for binding to the $S1P_1$/Edg1 receptor of 100 nM or less as evaluated by the ^{35}S-GTPγS binding assay,

with the proviso that the compound does not fall within formula A:



A

or a pharmaceutically acceptable salt or hydrate thereof, wherein:

X is O, S, NR^1 or $(CH_2)_{1-2}$, optionally substituted with 1-4 halo groups;

R^1 is H, C_{1-4}alkyl or haloC_{1-4} alkyl;

R^{1a} is H, OH, C_{1-4}alkyl, or OC_{1-4} alkyl, the alkyl and alkyl portions being optionally substituted with 1-3 halo groups;

R^{1b} represents H, OH, C_{1-4} alkyl or haloC_{1-4} alkyl;

each R^2 is independently selected from the group consisting of: H, C_{1-4} alkyl and haloC_{1-4} alkyl,

R^3 is H, OH, halo, C_{1-4}alkyl, OC_{1-4}alkyl, O-haloC_{1-4}alkyl or hydroxyC_{1-4}alkyl,

Y is selected from the group consisting of: $-CH_2-$, -C(O)-, -CH(OH)-, -C(=NOH)-, O and S, and

R^4 is selected from the group consisting of: C_{4-14}alkyl and C_{4-14}alkenyl.

47. The method according to Claim 46 wherein the compound has a selectivity for the $S1P_1$/Edg1 receptor over the $S1P_3$/Edg3 receptor of at least 100 fold as measured by the ratio of EC_{50} for the $S1P_1$/Edg1 receptor to the EC_{50} for the $S1P_3$/Edg3 receptor as evaluated in the ^{35}S-GTPγS binding assay.

48. The method according to Claim 47 wherein the compound has a selectivity for the $S1P_1$/Edg1 receptor over the $S1P_3$/Edg3 receptor of at least 200 fold as measured by the ratio of EC_{50} for the $S1P_1$/Edg1 receptor to the EC_{50} for the $S1P_3$/Edg3 receptor as evaluated in the ^{35}S-GTPγS binding assay.

49. The method according to Claim 48 wherein the compound has a selectivity for the $S1P_1$/Edg1 receptor over the $S1P_3$/Edg3 receptor of at least 500 fold as measured by the ratio of EC_{50} for the $S1P_1$/Edg1 receptor to the EC_{50} for the $S1P_3$/Edg3 receptor as evaluated in the ^{35}S-GTPγS binding assay.

50. The method according to Claim 49 wherein the compound has a selectivity for the $S1P_1$/Edg1 receptor over the $S1P_3$/Edg3 receptor of at least 2000 fold as measured by the ratio of EC_{50} for the $S1P_1$/Edg1 receptor to the EC_{50} for the $S1P_3$/Edg3 receptor as evaluated in the ^{35}S-GTPγS binding assay.

51. A method of treating a respiratory disease or condition in a mammalian patient in need of such treatment comprising administering to said patient a compound which is an agonist of the $S1P_1$/Edg1 receptor in an amount effective for treating said respiratory disease or condition, wherein said compound possesses a selectivity for the S1P1/Edg1 receptor over the $S1P_3$/Edg3 receptor of at least 100 fold as measured by the ratio of EC_{50} for the $S1P_1$/Edg1 receptor to the EC_{50} for the $S1P_3$/Edg3 receptor as evaluated in the ^{35}S-GTPγS binding assay and wherein said compound possesses an EC_{50} for binding to the $S1P_1$/Edg1 receptor of 10 nM or less as evaluated by the ^{35}S-GTPγS binding assay.

52. The method according to Claim 51 wherein the compound possesses an EC_{50} for binding to the $S1P_1$/Edg1 receptor of 1 nM or less as evaluated by the ^{35}S-GTPγS binding assay.

53. The method according to Claim 52 wherein the compound has a selectivity for the $S1P_1$/Edg1 receptor over the S1P3/Edg3 receptor of at least 200 fold as measured by the ratio of EC_{50} for the $S1P_1$/Edg1 receptor to the EC_{50} for the S1P3/Edg3 receptor as evaluated in the ^{35}S-GTPγS binding assay.

54. The method according to Claim 53 wherein the compound has a selectivity for the $S1P_1$/Edg1 receptor over the S1P3/Edg3 receptor of at least 500 fold as measured by the ratio of EC_{50} for the $S1P_1$/Edg1 receptor to the EC_{50} for the S1P3/Edg3 receptor as evaluated in the ^{35}S-GTPγS binding assay.

55. The method according to Claim 54 wherein the compound has a selectivity for the $S1P_1$/Edg1 receptor over the S1P3/Edg3 receptor of at least 1000 fold as measured by the ratio of EC_{50} for the $S1P_1$/Edg1 receptor to the EC_{50} for the S1PR3/Edg3 receptor as evaluated in the ^{35}S-GTPγS binding assay.

56. The method according to Claim 55 wherein the compound has a selectivity for the $S1P_1$/Edg1 receptor over the S1PR3/Edg3 receptor of at least 2000 fold as measured by the ratio of EC_{50} for the $S1P_1$/Edg1 receptor to the EC_{50} for the S1P3/Edg3 receptor as evaluated in the ^{35}S-GTPγS binding assay.

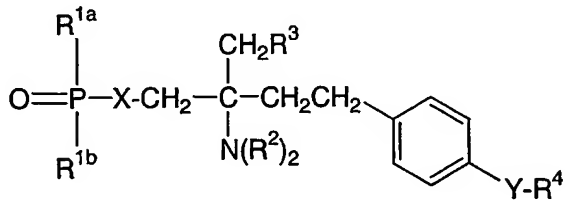
57. The method according to Claim 46 wherein the respiratory disease or condition is selected from the group consisting of: asthma, chronic bronchitis, chronic obstructive pulmonary disease, adult respiratory distress syndrome, infant respiratory distress syndrome, cough, eosinophilic granuloma, respiratory syncytial virus bronchiolitis, bronchiectasis, idiopathic pulmonary fibrosis, acute lung injury and bronchiolitis obliterans organizing pneumonia.

58. The method according to Claim 46 further comprising concomitantly or sequentially administering one or more agents selected from the

group consisting of: a Leukotriene receptor antagonist, a Leukotriene biosynthesis inhibitor, an M2/M3 antagonist, phosphodiesterase 4 inhibitor, calcium activated chloride channel 1 agonist, a corticosteroid, an H1 receptor antagonist, a beta 2 adrenoreceptor agonist and a prostaglandin D2 antagonist.

59. A method of modulating airway function in a mammalian patient in need thereof comprising administering to said patient a compound which is an agonist of the $S1P_1$/Edg1 receptor in an amount effective for modulating airway function, wherein said compound possesses a selectivity for the S1P1/Edg1 receptor over the S1PR3/Edg3 receptor of at least 20 fold as measured by the ratio of EC_{50} for the $S1P_1$/Edg1 receptor to the EC_{50} for the $S1P_3$/Edg3 receptor as evaluated in the ^{35}S-GTPγS binding assay and wherein said compound possesses an EC_{50} for binding to the $S1P_1$/Edg1 receptor of 100 nM or less as evaluated by the ^{35}S-GTPγS binding assay,

with the proviso that the compound does not fall within formula A:



A

or a pharmaceutically acceptable salt or hydrate thereof, wherein:

X is O, S, NR^1 or $(CH_2)_{1-2}$, optionally substituted with 1-4 halo groups;

R^1 is H, C_{1-4}alkyl or haloC_{1-4} alkyl;

R^{1a} is H, OH, C_{1-4}alkyl, or OC_{1-4} alkyl, the alkyl and alkyl portions being optionally substituted with 1-3 halo groups;

R^{1b} represents H, OH, C_{1-4} alkyl or haloC_{1-4} alkyl;

each R^2 is independently selected from the group consisting of: H, C_{1-4} alkyl and haloC_{1-4} alkyl,

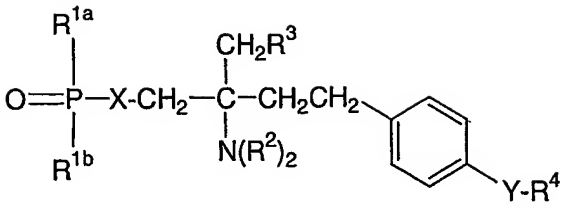
R^3 is H, OH, halo, C_{1-4}alkyl, OC_{1-4}alkyl, O-haloC_{1-4}alkyl or hydroxyC_{1-4}alkyl,

Y is selected from the group consisting of: $-CH_2-$, -C(O)-, -CH(OH)-, -C(=NOH)-, O and S, and

R^4 is selected from the group consisting of: C_{4-14}alkyl and C_{4-14}alkenyl.

60. A method of reducing or preventing the activation of the S1P1/Edg1 receptor in a mammalian patient in need thereof comprising administering to said patient a compound which is an agonist of the $S1P_1$/Edg1 receptor in an amount effective for reducing or preventing the activation of S1P1/Edg1 receptor, wherein said compound possesses a selectivity for the S1P1/Edg1 receptor over the $S1PR_3$/Edg3 receptor of at least 20 fold as measured by the ratio of EC_{50} for the $S1P_1$/Edg1 receptor to the EC_{50} for the $S1P_3$/Edg3 receptor as evaluated in the ^{35}S-GTPγS binding assay and wherein said compound possesses an EC_{50} for binding to the $S1P_1$/Edg1 receptor of 100 nM or less as evaluated by the ^{35}S-GTPγS binding assay,

with the proviso that the compound does not fall within formula A:



A

or a pharmaceutically acceptable salt or hydrate thereof, wherein:

X is O, S, NR^1 or $(CH_2)_{1-2}$, optionally substituted with 1-4 halo groups;

R^1 is H, C_{1-4}alkyl or haloC_{1-4} alkyl;

R^{1a} is H, OH, C_{1-4}alkyl, or OC_{1-4} alkyl, the alkyl and alkyl portions being optionally substituted with 1-3 halo groups;

R^{1b} represents H, OH, C_{1-4} alkyl or haloC_{1-4} alkyl;

each R^2 is independently selected from the group consisting of: H, C_{1-4} alkyl and haloC_{1-4} alkyl,

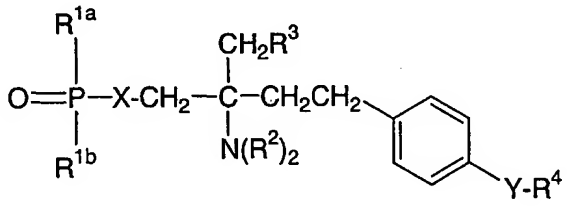
R^3 is H, OH, halo, C_{1-4}alkyl, OC_{1-4}alkyl, O-haloC_{1-4}alkyl or hydroxyC_{1-4}alkyl,

Y is selected from the group consisting of: $-CH_2-$, -C(O)-, -CH(OH)-, -C(=NOH)-, O and S, and

R^4 is selected from the group consisting of: C_{4-14}alkyl and C_{4-14}alkenyl.

61. A method of inhibiting an infiltration of a lymphocyte into a respiratory tissue in a mammalian patient in need thereof by promoting a sequestration of the lymphocyte in a lymph node thereby preventing release of a pro-inflammatory mediator in the respiratory tissue comprising administering to said patient a compound which is an agonist of the $S1P_1$/Edg1 receptor in an amount effective for modulating airway function, wherein said compound possesses a selectivity for the S1P1/Edg1 receptor over the $S1PR_3$/Edg3 receptor of at least 20 fold as measured by the ratio of EC_{50} for the $S1P_1$/Edg1 receptor to the EC_{50} for the $S1P_3$/Edg3 receptor as evaluated in the ^{35}S-GTPγS binding assay and wherein said compound possesses an EC_{50} for binding to the $S1P_1$/Edg1 receptor of 100 nM or less as evaluated by the ^{35}S-GTPγS binding assay,

with the proviso that the compound does not fall within formula A:



A

or a pharmaceutically acceptable salt or hydrate thereof, wherein:

X is O, S, NR^1 or $(CH_2)_{1-2}$, optionally substituted with 1-4 halo groups;

R^1 is H, C_{1-4}alkyl or haloC_{1-4} alkyl;

R^{1a} is H, OH, C_{1-4}alkyl, or OC_{1-4} alkyl, the alkyl and alkyl portions being optionally substituted with 1-3 halo groups;

R^{1b} represents H, OH, C_{1-4} alkyl or haloC_{1-4} alkyl;

each R^2 is independently selected from the group consisting of: H, C_{1-4} alkyl and haloC_{1-4} alkyl,

R^3 is H, OH, halo, C_{1-4}alkyl, OC_{1-4}alkyl, O-haloC_{1-4}alkyl or hydroxyC_{1-4}alkyl,

Y is selected from the group consisting of: $-CH_2-$, -C(O)-, -CH(OH)-, -C(=NOH)-, O and S, and

R^4 is selected from the group consisting of: C_{4-14}alkyl and C_{4-14}alkenyl.